The bite of an Aedes mosquito carrying any one of the four dengue viral serotypes causes dengue fever, an acute febrile viral illness. The majority of the world's population is in danger, particularly in countries with tropical and subtropical climates like Bangladesh. All of the country's districts are impacted by the geographical spread of cases reported in 2019 that has occurred the most frequently; it clearly favors men and predominantly affects younger persons. The Ministry of Health & Family Welfare of Bangladesh has reported a total of 3290 laboratory-confirmed dengue cases and 26 associated deaths from 1 January to 12 June 2023. Dhaka is the division that is most severely impacted, with 78%(n=2562) of cases and 60.4% of fatalities. We must emphasize how serious the current epidemic is. Sadly, the authorities are handling it very carelessly, as evidenced not only by the glaring underreporting but also by the lack of public health awareness campaigns aimed at both the general public and medical professionals. These initiatives, which focus on earlier and more consistent diagnosis of dengue infections and supportive clinical management of those cases, are urgently required since they significantly reduce mortality for this highly contagious disease (2). There is very little information in the literature regarding the relationship between the demographic profile, clinical characteristics, comorbidities, and the prognosis/complications of dengue in Bangladesh. The association will aid in identifying dengue patients who are at high risk. Different warning indicators can be utilized to identify potentially serious cases early, allowing for prompt treatment, preventing unneeded hospital stays, and lowering the disease's case fatality rate. However, several clinical and epidemiological aspects, particularly in Bangladesh, have not yet been fully clarified. Therefore, the purpose of this study is to comprehend the relationship between various clinical characteristics and comorbidities. However, as Dhaka is the largest city in Bangladesh and has seen 70% of dengue cases, 60% of which resulted in fatalities in the past year, we only select the Dhaka division.

**Research question:**

1. What is the link between pre-existing medical conditions and the occurrence of severe dengue?
2. How are the clinical symptoms and laboratory test results upon admission related to the development of severe dengue?

**Methodology:**

**Case Definition:**

Based on the 2009 World Health Organization (WHO) Dengue Case Classification, which includes laboratory-confirmed dengue or probable dengue, this study diagnosed dengue. Positive results for NS1 obtained with quick dengue diagnostic kits will allow for the identification of laboratory-confirmed dengue cases. The WHO 2009 criteria for probable dengue, which include fever associated with at least two of the following symptoms—nausea or vomiting, rash, aches and pains, a positive tourniquet test, leukopenia, and any warning signs—will be used to diagnose probable dengue patients. A positive Dengue IgM antibody in a serum sample collected during the late-acute or convalescent phase was required in addition to clinical criteria for probable dengue cases. Dengue diagnostic kits will be used to get dengue serology results (IgM or IgG). According to the rules issued by the WHO in 2009, severe dengue was defined.

**Study design and sample size:**

This case-control study will be carried out at Dhaka Medical College Hospital (DMCH) in Dhaka, Bangladesh. The ninth floor of DMCH includes a special section for treating and caring for dengue patients. Because of the high frequency of dengue illnesses this year, which is likely related to unusually heavy rains and temperature since June 2023, participants will be gathered between January 1 and June 15, 2023. Using Sample Size, an online sample size calculator, the sample size will be estimated at 435 individuals. (<https://sampsize.sourceforge.net/>). In this case-control study, we considered 80% power, 95% level of confidence, 7% exposure among controls, an odds ratio (OR) of 2.5, and a 1:2 allocation ratio for each group. We calculated that we would need 435 patients, made up of 145 cases and 290 controls. Diabetes mellitus, the comorbidity with the smallest prevalence among those being investigated, is prevalent in the Bangladeshi community, hence the percentage of exposed controls will be set at7%.(<http://bbs.portal.gov.bd/sites/default/files/files/bbs.portal.gov.bd/page/4c7eb0f0_e780_4686_b546_b4fa0a8889a5/HMSS.pdf>). Based on a prior study by Badawi et al., who found that patients with comorbidities such as diabetes, hypertension, and heart disease had chances ratios of severe dengue that ranged from 2 to 4 patients, the odds ratio of 2.0 will be used. (<https://europepmc.org/article/med/29990356>). A case-control ratio of 1:2 would be set in order to increase precision while taking feasibility into account. Using criteria such as gender, age group (within a 5-year range of the case's age), and hospital admission date (within a 2-week window of the patient's admission date), controls will be chosen from patients admitted to the general medical ward and matched to the cases.

Up to five relevant controls will be taken into consideration when there are several alternative controls that might be used. The randomization tool will then be used to choose the top two controls at random to reduce selection bias. Due to practical concerns, the maximum number of potential controls will be five. To account for any differences in results across various age groups and genders age- and sex-based matching will be used. To avoid confounding factors associated with differences in circulating dengue serotypes, matching according to hospital admission dates will also be deemed required.

**Variables:**

**Dependent variable:**

Severe dengue (Yes or No)

**Independent Variables:**

The original medical case notes and the patients' hematology/biochemical test reports will be used to retrospectively collect all pertinent clinical data. The extracted information included demographic details (age, gender, ethnicity, nationality, height, weight), pre-existing medical conditions (obesity, diabetes mellitus, hypertension, hyperlipidemia, chronic kidney disease, chronic pulmonary disease (including asthma or chronic obstructive pulmonary disease), and stroke), presenting signs and symptoms (fever, abdominal pain, diarrhea, vomiting, lethargy, musculoskeletal (MSK) symptoms (such as myalgia, arthralgia, or bone pain), chills or rigors, upper respiratory tract infection (URTI) symptoms (such as a runny nose, sore throat, or cough), bleeding manifestations (such as gum bleeding, nosebleeds, hemoptysis, hematemesis, melaena, or vaginal bleeding), headache, and skin rash), and hematological/biochemical laboratory parameters (hemoglobin (Hb), hematocrit (Hct), white cell count (WCC), and platelet count, while the biochemical laboratory results included urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, creatine kinase (CK), and lactate dehydrogenase (LDH)) upon admission. According to the WHO Guidelines, obesity was classified as having a body mass index (BMI) of 27.5 kg/m2 or higher based on admission data. Other comorbidities will be noted based on the formal diagnosis provided in the patient records.

**Statistical Analysis:**

All variables will be entered into Microsoft Excel and analyzed with the R program. Demographics, comorbidities, presenting signs and symptoms, and admission laboratory results will all be compared between cases and controls. If the Kolmogorov-Smirnov test confirms that a continuous variable has a non-normal distribution, it will be reported as the median and interquartile range (IQR), otherwise, the mean and standard deviation (SD) will be used.

Using Fisher's exact test or Pearson's chi-square, descriptive studies compared categorical variables. The Wilcoxon rank-sum test (also known as the Mann-Whitney U test) will be applied for analysis if our continuous variables do not have a normal distribution.

The matching criteria (age, gender, and admission date) from our study will be taken into consideration in the inferential analysis using a matched case-control design and conditional logistic regression. The conditional odds ratio (COR) will be calculated using a univariate conditional logistic regression, and the adjusted conditional odds ratio (AcOR), which considers potential confounders, will be calculated using a multivariable conditional logistic regression. The confounding effect will be minimized by adjusting for potential confounders identified during the univariate analysis. Variables with statistically significant differences (p<0.05) between cases and controls in the descriptive analysis will be considered potential confounders.

**Expected outcomes**

Significant association with severe dengue cases and comorbidities between adult patients. We also hypothesize the association between pre-existing medical conditions, clinical symptoms, laboratory test results upon admission, and the development of severe dengue.